

Application No. 09/960,612

Reply to Office Action dated April 9, 2003

Amendments to the Claims:

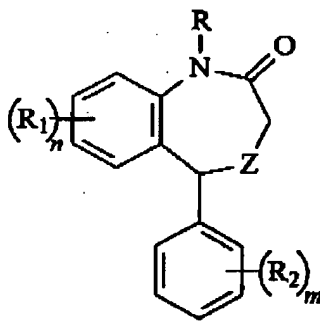
This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1. (Currently Amended) A method for treating diabetes mellitus, comprising:

administering, to a subject having or suspected of being at risk for having diabetes mellitus, a therapeutically effective amount of a pharmaceutical composition comprising an agent that selectively impairs a mitochondrial calcium/ sodium antiporter activity in an insulin secreting cell:

wherein the agent has the following structure:



or a stereoisomer, prodrug or pharmaceutically acceptable salt thereof

wherein

Z is O, S, S(=O) or S(=O)₂;

R is hydrogen, alkyl or substituted alkyl;

R₁ and R₂ are the same or different and at each occurrence are independently halogen, cyano, nitro, mono- or di-alkylamino, alkyl, substituted alkyl, aryl, substituted aryl, arylalkyl, substituted arylalkyl, heterocycle, substituted heterocycle, heterocyclealkyl or substituted heterocyclealkyl; and

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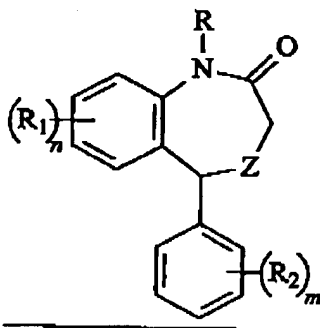
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n and m are the same or different, and independently 0, 1, 2, 3 or 4.

2. (Currently Amended) A method for treating diabetes mellitus, comprising:

administering, to a subject having or suspected of being at risk for having diabetes mellitus, a therapeutically effective amount of a pharmaceutical composition comprising an agent that selectively impairs a mitochondrial calcium/ sodium antiporter activity in an insulin secreting cell wherein said agent enhances insulin secretion:

and wherein the agent has the following structure:



or a stereoisomer, prodrug or pharmaceutically acceptable salt thereof.

wherein

Z is O, S, S(=O) or S(=O)₂;

R is hydrogen, alkyl or substituted alkyl;

R₁ and R₂ are the same or different and at each occurrence are independently halogen, cyano, nitro, mono- or di-alkylamino, alkyl, substituted alkyl, aryl, substituted aryl, arylalkyl, substituted arylalkyl, heterocycle, substituted heterocycle, heterocyclealkyl or substituted heterocyclealkyl; and

n and m are the same or different, and independently 0, 1, 2, 3 or 4.

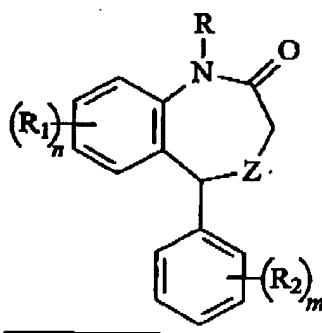
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3. (Currently Amended) A method for treating diabetes mellitus, comprising:

administering, to a subject having ~~orsuspected~~ of being at risk for having diabetes mellitus, a therapeutically effective amount of a pharmaceutical composition comprising an agent that selectively impairs a mitochondrial calcium/ sodium antiporter activity in an insulin secreting cell wherein said agent enhances insulin secretion that is stimulated by glucose:

and wherein the agent has the following structure:



or a stereoisomer, prodrug or pharmaceutically acceptable salt thereof

wherein

Z is O, S, S(=O) or S(=O)₂;

R is hydrogen, alkyl or substituted alkyl;

R₁ and R₂ are the same or different and at each occurrence are independently halogen, cyano, nitro, mono- or di-alkylamino, alkyl, substituted alkyl, aryl, substituted aryl, arylalkyl, substituted arylalkyl, heterocycle, substituted heterocycle, heterocyclealkyl or substituted heterocyclealkyl; and

n and m are the same or different, and independently 0, 1, 2, 3 or 4.

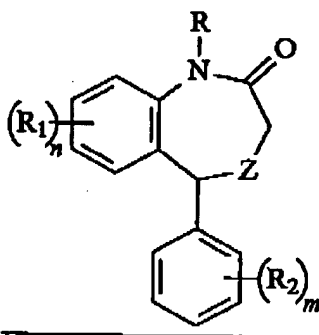
4. (Currently Amended) A method for treating diabetes mellitus, comprising:

administering, to a subject having ~~orsuspected~~ of being at risk for having diabetes mellitus, a therapeutically effective amount of a pharmaceutical composition comprising an

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agent that selectively impairs a mitochondrial calcium/sodium antiporter activity in an insulin secreting cell wherein said agent enhances insulin secretion that is stimulated by a supraphysiological glucose concentration and does not enhance insulin secretion in the presence of a fasting physiological glucose concentration and wherein the agent has the following structure:



or a stereoisomer, prodrug or pharmaceutically acceptable salt thereof,

wherein

Z is O, S, S(=O) or S(=O)₂;

R is hydrogen, alkyl or substituted alkyl;

R₁ and R₂ are the same or different and at each occurrence are independently halogen, cyano, nitro, mono- or di-alkylamino, alkyl, substituted alkyl, aryl, substituted aryl, arylalkyl, substituted arylalkyl, heterocycle, substituted heterocycle, heterocyclealkyl or substituted heterocyclealkyl; and

n and m are the same or different, and independently 0, 1, 2, 3 or 4.

5. (Original) The method of any one of claims 1-4 wherein the diabetes mellitus is type 2 diabetes mellitus.

6. (Original) The method of any one of claims 1-4 wherein the diabetes mellitus is maturity onset diabetes of the young.

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7. (Original) The method of any one of claims 1-4 wherein the pharmaceutical composition is administered orally.

8. (Original) The method of any one of claims 1-4 wherein the agent does not substantially alter insulin secretion in the presence of a fasting physiological glucose concentration.

9. (Previously Presented) The method of any one of claims 1-4 wherein the agent is membrane permeable.

10. (Original) The method of claim 9 wherein the membrane is at least one of the membranes selected from the group consisting of a plasma membrane and a mitochondrial membrane.

11. (Original) The method of claim 10 wherein the mitochondrial membrane is selected from the group consisting of an inner mitochondrial membrane and an outer mitochondrial membrane.

12.-26. (Canceled)

27. (Currently Amended) The method of ~~claim 25~~any one of claims 1-4 wherein Z is sulfur.

28. (Currently Amended) The method of ~~claim 25~~any one of claims 1-4 wherein n is 1.

29. (Currently Amended) The method of ~~claim 25~~any one of claims 1-4 wherein m is 1.

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30. (Original) The method of claim 28 wherein R_1 is halogen.
31. (Original) The method of claim 29 wherein R_2 is halogen.
32. (Original) The method of claim 30 wherein R_1 is halogen at the 8-position.
33. (Original) The method of claim 31 wherein R_2 is halogen at the 2-position.
34. (Original) The method of ~~claim 25~~any one of claims 1-4 wherein R is hydrogen.
- 35.-40. (Canceled)